

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendments, claims 43, 44, 46, 48-50, 52-57, 59-61, 63 and 64 are pending in the application, with claims 43, 52 and 63 being the independent claims. Claim 52 has been amended. Support the amendment can be found in the specification as filed as well as the originally filed claims. In light of the following remarks, Applicants respectfully request reconsideration of the application, withdrawal of the finality of the Office Action dated May 18, 2005, entry of this response and allowance of the pending claims to issue.

***Objection to the Specification***

In the Office Action at pages 2-3, the Examiner has maintained the objection to the specification. Specifically, with regard to the statement in the present specification incorporating by reference all publications, patents and patent applications mentioned in the specification, the Examiner states: "[s]uch omnibus language fails to specify what specific information applicant seeks to incorporate by reference and similarly fails to teach with detailed particularity just where that specific information is to be found in each of the cited documents." Office Action at page 2, lines 14-16. The Examiner therefore concludes "[a]ccordingly, the cited documents are not considered to have been properly incorporated by reference and as such, have not been considered with any effect towards their fulfilling, either in part or in whole, the enablement, written description, or best mode requirements of 35 U.S.C. § 112, first paragraph." Office Action at page 3, lines 18-21. Solely in an effort to expedite prosecution, and without acquiescing with the

propriety of the objection, Applicants have amended the specification herein to remove the statement "All publications, patents applications and patents cited herein are fully incorporated by reference herein in their entirety." Thus, the objection to the specification is now moot. Reconsideration and withdrawal of the objection to specification are therefore respectfully requested.

***Objections to the Claims***

In the Office Action at page 5, the Examiner objected to claim 52 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Specifically, the Examiner alleges:

Claim 43 sets that the range in size of the fragments is to be from "about 25 kb to about 100 bp," however, claim 52 stipulates that the fragments of the composition are to "differ in length by increments of about 1,000 base pairs." It is not possible to have fragments of either 25 KB or 100 BP and at the same time vary the fragment lengths in units of 1,000. Accordingly, such a limitation effectively broadens the scope of claim 43, not further limit it.

Office Action at page 5, lines 8-14. Solely in an effort to expedite prosecution, and without acquiescing with the propriety of the objection, Applicants have amended claim 52 to be in independent form. Thus, the objection of claim 52 is now moot. Reconsideration and withdrawal of the objection to claim 52 are therefore respectfully requested.

***Rejections under 35 U.S.C. § 103***

In the Office Action on page 6, section 10, the Examiner rejected claims 43, 44, 46, 48-50, 52-56, 59-60, 63, and 64 under 35 U.S.C. § 103(a) as being unpatentable over

Life Technologies Catalogue (1995-1996) in view of Stratagene Cloning Systems Catalogue (Stratagene; 1993). The Examiner contends that it would have been obvious to one of ordinary skill in the art to have developed any of a variety of DNA ladders for use in an electrophoresis assay and to have adjusted the relative concentrations of the bands such that the intensities of any one or all of the bands was the same or more intense than the other bands. *See* Office Action at pages 7-8. section 15. Applicants respectfully traverse this rejection and reiterate and incorporate by reference the remarks made in the Applicants' previous replies concerning this rejection. Applicants also wish to provide the additional following remarks.

Establishing *prima facie* obviousness requires a showing that each claim element is taught or suggested by the prior art. *See In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Specifically, establishing *prima facie* obviousness requires a showing that some combination of objective teachings in the art and/or knowledge available to one of skill in the art would have led that individual to arrive at the claimed invention. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988).

As specifically noted by the Examiner in the Office Action at page 7, section 13, Life Technologies Catalogue (1995-1996) does not "teach of a ladder that has an upper limit of 25 kb." In addition, a careful examination of the DNA ladders on pages 14-2 through 14-4 of the Life Technologies Catalogue reveals that all of the listed DNA ladders display bands having substantial variance in intensity among the individual bands within each ladder. Applicants further direct the Examiner's attention to Figure 2 and pages 21-22 of the original specification. Figure 2 illustrates the differences between the present invention and various commercially available DNA ladders when analyzed by

gel electrophoresis. Specifically, Lane 2 of Figure 2 contains the 1 kb ladder that is disclosed in Life Technologies Catalogue (1995-1996) at page 14-4 and which is specifically cited by the Examiner at page 6, section 12 of the Office Action. Contrary to the Examiner's statement, analysis of the 1 kb ladder actually shows that fragments of the 1kb ladder smaller than 1 kb appear substantially less intense than the 1018 bp increment band. In fact, the bands smaller than 1 kb are so much less intense than the other bands within the ladder that the bands are barely, if at all, visible. This is because the relative mass of each of these fragments (and thus the intensity of these bands when stained) decreases in proportion to its size. Thus, it is not "readily apparent that the individual bands in the 1 kb ladder also appear to be at the same relative intensity," as alleged by the Examiner. As such, Life Technologies Catalogue is deficient in teaching or suggesting the ladders as presently claimed, which consist essentially of a plurality of double-stranded DNA fragments ranging in *length from about 25 kb to about 100 bases* present in an amount that produces bands of *substantially equal intensity* after the composition is separated by gel electrophoresis and stained with a detectable label.

The Examiner attempts to cure the deficiencies of Life Technologies Catalogue by combining its deficient disclosure with Stratagene Cloning Systems Catalogue (Stratagene; 1993). Specifically, the Examiner states that "Stratagene, page 122, teaches DNA ladders that range from about 400 bp to about 48 kb." Applicants respectfully disagree with the Examiner's conclusion. Stratagene merely provides "[t]he FLASH<sup>®</sup> non-radioactive marker is designed to be used in conjunction with the FLASH<sup>®</sup> detection system for sizing DNA using a non-radioactive system. The biotinylated FLASH marker yields 26 bands suitable for sizing linear DNA from 60 bp to 48.5 kb." Thus, it is

completely void of any disclosure regarding the presence of bands of substantially equal intensity, as required by the claims of the present invention. Moreover, the photograph of the ladder shown on page 122 of the Stratagene Catalogue explicitly shows that the bands ranging from about 22 kb to about 4 kb are substantially more intense than the bands smaller than 2 kb. Thus, Stratagene; 1993, alone or in combination with Life Technologies Catalogue, fails to teach or suggest double-stranded DNA fragments ranging in length from about 25 kb to about 100 bases present in an amount that produces bands of *substantially equal intensity* after the composition is separated by gel electrophoresis and stained with a detectable label. As such, Life Technologies Catalogue (1995-1996) in view of Stratagene Cloning Systems Catalogue (Stratagene; 1993) does not render the present invention obvious.

The Examiner, upon seemingly realizing the deficient disclosures of the cited art, attempts to cure these deficiencies by alleging that:

In the event that the applicant considers the prior art as not teaching the generation of bands that will have substantially the same intensity, it is the position that such a property is the result of routine optimization and does not rise to the level of a patentable distinction.

Office Action, page 7, section 14, lines 5-7. Applicants disagree with the Examiner's unsupported conclusory statement and assert that his reliance thereon to establish a case of obviousness is improper.

As stated *supra*, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. See *In re Piasecki*, 745 F.2d 1468, 1471-73 (Fed. Cir. 1984). To meet this burden, the Examiner must satisfy three requirements. First, all of the claim limitations must be taught or suggested by the prior art. See *In re Royka*, 490 F.2d 981, 984-85 (CCPA 1974); see also *In re Glaug*, 283 F.3d 1335, 1341-42 (Fed.

Cir. 2002) (finding a claim not obvious because the prior art did not teach "spaced zones of adhesive" as recited in the claim); *In re Rijckaert*, 9 F.3d 1531, 1533 (Fed. Cir. 1993) (finding a claim not obvious because the prior art did not teach all claim limitations). Second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *See In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998). Third, there must be a reasonable expectation of success. *See In re Merck & Co., Inc.*, 800 F.2d 1091 (Fed. Cir. 1986). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicants' disclosure. *See In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

As explained above, the Examiner has failed to meet his burden of establishing an *prima facie* case of obviousness because the cited art does not teach or suggest a DNA Ladder ranging in length from about 25 kb to about 100 bases present in an amount that produces bands of *substantially equal intensity*. Likewise, the Examiner's conclusory statement regarding "routine optimization" fails to satisfy the requirements of a *prima facie* case of obviousness. The Examiner has provided no support for the allegation that "such a property is the result of routine optimization." Moreover, the Examiner has failed to show any suggestion or motivation to modify the cited references, or to combine their teachings with a reasonable expectation of success in arriving at the claimed invention. Applicants further assert that it is clear from the disclosure of the specification that this invention was not the result of routine optimization and thus, this general statement

contributes nothing to further support the Examiner's allegation that the disclosure of Stratagene renders the claimed invention obvious.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 43, 44, 46, 48-50, 52-56, 59-60, 63, and 64 under 35 U.S.C. § 103(a) as being unpatentable over Life Technologies Catalogue (1995-1996) in view of Stratagene Cloning Systems Catalogue (Stratagene; 1993).

In the Office Action on page 8, section 16, the Examiner rejected claims 57 and 61 under 35 U.S.C. § 103(a) as being unpatentable over Life Technologies Catalogue (1995-1996) in view of Stratagene Cloning Systems Catalogue (Stratagene; 1993) as applied to claims 43, 44, 46, 48-50, 52-56, 59-60, 63, and 64, and further in view of Lee (U.S. Patent No. 5,268,568). Specifically, the Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the DNA ladders of Life Technologies such that a dye comprising bromophenol blue was included given its common usage in electrophoresis of DNA samples. Applicants respectfully traverse this rejection and reiterate and incorporate by reference the remarks made in the Applicants' previous replies concerning this rejection.

As detailed above, the Life Technologies Catalogue (1995-1996) in view of the Stratagene Cloning Systems Catalogue fails to disclose or suggest "bands of substantially equal intensity," which is a required limitation of claims 57 and 61 based upon their dependence on claim 43. Lee does not cure this defect. Therefore a key limitation in claims 57 and 61 is not taught or suggested by the combination of the Life Technologies Catalogue (1995-1996) in view of Stratagene Cloning Systems Catalogue and further in

view of Lee. Furthermore, because the claimed composition of the present application is non-obvious, the kit comprising the composition is also necessarily non-obvious.

In view of the foregoing remarks, Applicants respectfully request that the rejection of claim 57 and 61 under 35 U.S.C. § 103(a) over Life Technologies Catalogue (1995-1996) in view of Stratagene Cloning Systems Catalogue (Stratagene; 1993) as applied to claims 43, 44, 46, 48-50, 52-56, 59-60, 63, and 64, and further in view of Lee (U.S. Patent No. 5,268,568) be reconsidered and withdrawn.



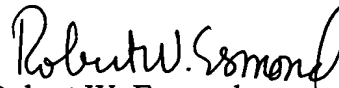
***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

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